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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,815	04/10/2006	Jae Yong Han	50413/012001	6292

21559 7590 01/31/2008  
CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

EXAMINER
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LONG, SCOTT

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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01/31/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

## Office Action Summary

**Application No.**

10/567,815

**Applicant(s)**

HAN ET AL.

**Examiner**

Scott D. Long

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 2/9/2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Claim Status***

Claims 1-15 are pending. Claims 1-15 are under current examination.

### ***Oath/Declaration***

The oath or declaration, having the signatures of all inventors, received on 10 April 2006 is in compliance with 37 CFR 1.63.

### ***Information Disclosure Statement***

The Information Disclosure Statements (IDS) filed on 9 February 2006 consisting of 1 sheet(s) are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

### ***Priority***

This application claims benefit as a 371 of PCT/KR04/02018 (filed 08/11/2004). This application also claims benefit from foreign application REPUBLIC OF KOREA 10-2003-0055326 (filed 11 August 2003). The instant application has been granted the benefit date, 11 August 2003, from foreign application REPUBLIC OF KOREA 10-2003-0055326.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 recites the limitation "The avian" in the preamble of claim 14. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 10, and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin (US2002/0076797, published 20 June 2002).

Claim 1 is directed to a method for producing an avian chimera using spermatogonial cells, which comprises the steps of: (a) retrieving a testis from a donor ave; (b) isolating a testicular cell population from said testis; (c) culturing said testicular cell population in a medium supplemented with a cell growth factor to obtain a spermatogonial cell population and (d) injecting said cultured spermatogonial cell population of said testicular cell population into a testis of a recipient ave to produce

said avian chimera. Lin teaches "production of chimeric animals, including transgenic chimeric animals...particularly chimeric or transgenic chimeric avians" (page 13, parag.0128). Lin teaches genes "from warm blooded vertebrates re-introduced into isolated spermatogonial cells or other relevant cells. The re-injection of the transgene-carrying cells into the testis or other relevant tissues...." (page 21, parag.0209). The instant specification teaches, "[t]he term 'testicular cell' used herein refers to a population of cells present in the testicular tissue, including spermatogonial stem cells, spermatogonial cells....This term is used interchangeably with the term 'testicular cell population'" (Spec., page 8, lines 10-16). Lin teaches, culture of primitive cells (page 12, parag.0115) in culture media or via a feeder matrix (page 12, col.0119) and further describe "a feeder matrix can be derived from or provided by the organ or tissue in which the primitive cells are located, e.g., the gonad" (page 13, parag.0120). The method of Lin also comprises "collecting primitive cells" (page 12, parag.0119). The examiner interprets the teachings of Lin to mean that primitive cells (e.g., germline stem cells) (page 12, parag.0115) were collected from testis and cultured in medium supplemented with growth factors (page 2, parags.0011-0012). While it is clear that Lin teaches the general method of claim 1, the particular limitation of "retrieving a testis from a donor ave" is not explicitly taught. However, the examiner believes this limitation to be inherent in the teachings of Lin as described above; in order to collect the primitive cells from the gonad of an ave, Lin would have followed the standard art recognized procedures of retrieving the testis.

Claim 3 is directed to the method of claim 1, wherein said cell growth factor is selected from the group consisting of fibroblast growth factor, insulin-like growth factor-1, stem cell factor and combination thereof. Lin teaches "media used in carrying out the present invention may be any suitable media....The media can be supplemented with growth factors, including...insulin-like growth factor (IGF), fibroblast growth factor (FGF)...stem cell factor" (page 13, parag.0125).

Claims 4-5 are directed to the method of claim 1, wherein said medium further comprises a differentiation inhibitory factor (claim 4), particularly leukemia inhibitory factor (claim 5). Lin teaches "The media can be supplemented with growth factors, including...leukemia inhibitory factor (LIF)" (page 13, parag.0125).

Claim 6 is directed to the method of claim 1 wherein said medium contains a supplement comprising a mixture of fibroblast growth factor, insulin-like growth factor-1, and leukemia inhibitory factor. Lin teaches "The media can be supplemented with growth factors, including... leukemia inhibitory factor (LIF), insulin-like growth factor (IGF), fibroblast growth factor (FGF)" (page 13, parag.0125).

Claim 10 is directed to the method of claim 1, wherein said ave is selected from the group consisting of a chicken, a quail, a turkey, a duck, a goose, a pheasant or a pigeon. Lin teaches the avian species considered in his methods are: chicken, quail, turkey, duck, goose, and pheasant. (page 14, parag.0135).

Claim 12 is directed to the method of claim 1, wherein said method further after the step (d) comprises the step of conducting a testcross to verify whether said recipient

injected with said cultured spermatogonial cell population is chimera. Lin teaches backcrossing, intercrossing, test and control crossing to determine chimerism.

Claim 13 is directed to an avian chimera characterized in that it maintains spermatogonial cells of a donor in its testis, it has the ability to produce spermatozoa from said spermatogonial cells and said spermatozoa undergo a germline transmission into progenies. Lin teaches chimera that have spermatozoa which permit germline transmission to progeny.

Claim 14 is directed to an avian chimera according to claim 13, wherein said avian chimera is produced by any one of the methods of claims 1 to 11. Lin et al. teaches all the limitations of claim 1, thereby producing a chimeric ave.

Claim 15 is directed to a method for producing a transgenic ave, which comprises the steps of: (a) retrieving a testis from a donor ave; (b) isolating a testicular cell population from said testis; (c) culturing said testicular cell population in a medium supplemented with a cell growth factor to obtain a spermatogonial cell population; (c') transferring a foreign gene into said cultured spermatogonial cell population or testicular cell population; (d) injecting said cultured spermatogonial cell population or testicular cell population into a testis of a recipient ave; and (e) producing a progeny from said recipient to obtain said transgenic ave. Lin teaches "production of chimeric animals, including transgenic chimeric animals...particularly chimeric or transgenic chimeric avians" (page 13, parag.0128). Lin teaches genes "from warm blooded vertebrates re-introduced into isolated spermatogonial cells or other relevant cells. The re-injection of the transgene-carrying cells into the testis or other relevant tissues...." (page 21,

parag.0209). The instant specification teaches, "[t]he term 'testicular cell' used herein refers to a population of cells present in the testicular tissue, including spermatogonial stem cells, spermatogonial cells....This term is used interchangeably with the term 'testicular cell population'" (Spec., page 8, lines 10-16). Lin teaches, culture of primitive cells (page 12, parag.0115) in culture media or via a feeder matrix (page 12, col.0119) and further describe "a feeder matrix can be derived from or provided by the organ or tissue in which the primitive cells are located, E.g., the gonad" (page 13, parag.0120). The method of Lin also comprises "collecting primitive cells" (page 12, parag.0119). The examiner interprets the teachings of Lin to mean that primitive cells (e.g., germline stem cells) (page 12, parag.0115) were collected from testis and cultured in medium supplemented with growth factors (page 2, parags.0011-0012). While it is clear that Lin teaches the general method of claim 1, the particular limitation of "retrieving a testis from a donor ave" is not explicitly taught. However, the examiner believes this limitation to be inherent in the teachings of Lin as described above; in order to collect the primitive cells from the gonad of an ave, Lin would have followed the standard art recognized procedures of retrieving the testis. The result of practicing the method of Lin is a transgenic chimeric ave.

Accordingly, Lin anticipated the instant claims.



***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin (US2002/0076797, published 20 June 2002) in view of Rapp et al. (US2003/0126629, published 3 July 2003) and further in view of Li et al. (2002 Poultry Science; 81:1360-1364).

The teachings of Lin are recited above in the 35 USC 102 section. Lin teaches all the limitations of claims 1, 3-6, 10, and 12-15.

Lin does not explicitly teach the limitations of claims 2, 7-9 and 11.

The remaining claims are directed to further limitations of the method of claim 1, wherein the testis is digested with collagenase, trypsin or a mixture thereof (claim 2), and wherein said medium further comprises a serum and an antioxidant (claim 7) and wherein the donor cells are injected into the recipient's seminiferous tubule (claim 8), specifically the most upper portion of the seminiferous tubule (claim 9). In addition, claim 11 is directed to the method of claim 1, wherein said donor and said recipient are different species.

Rapp et al. teach an "in vitro, method of incorporating heterologous genetic material into the genome of an avian involves isolating male germ cells ex corpora, delivering a polynucleotide thereto and then returning the transfected cells to the testes of a recipient male bird." (page 15, parag.0152). Rapp et al. teach an embodiment which "employs injection of the gene delivery mixture, preferably into the seminiferous tubules, or into the pete testis, and most preferably into the vas efferens or vasa efferentia" (page 15, parag.0154) which encompasses the most upper portion of the seminiferous tubule. Rapp et al. also teach, "When the male germ cells are obtained from the donor vertebrate by transection of the testes, the cells can be incubated in an enzyme mixture known for gently breaking up the tissue matrix and releasing undamaged cells such as, for example, pancreatic trypsin, collagenase type I" (page 15, parag.0156). In addition Rapp et al. teach culture of these dispersed cells in DMEM medium with bovine serum albumin, as is standard tissue culture practice.

While Rapp et al. essentially teaches methods of transgenesis which use male germ line cells to deliver exogeneous nucleic acids, the methods share many similar teachings in common with Lin.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Lin with those of Rapp et al. to generate a method of producing transgenic chimeric fowl in which cultured male germ cells use standard tissue culture conditions and reagents, and in which methods of injecting the transformed male germ cells into the testes are injected into the seminiferous tubule of the recipient bird. In addition, Rapp et al. teach detailed methods of isolating testicular cell populations which use collagenase and trypsin to digest an isolated testis.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (method for producing an avian chimera using spermatogonial cells; injection of spermatogonial cells into the seminiferous tubule; methods of tissue culture for of spermatogonial stem cell) are taught by Lin or Rapp et al. and further they are taught in various combinations and are shown to be used in methods of creating transgenic chimeric ave. It would be therefore predictably obvious to use a combination of these three elements in a method for producing an avian chimera using

spermatogonial cells. The methods of tissue culture which use anti-oxidants (claim 7) such as  $\beta$ -mercaptoethanol are further known in the art and are predictable; therefore they are likewise obvious.

Regarding the limitations of claim 11, directed to a method for creating chimeric avians comprising different species (e.g., chicken-duck, chicken-quail, etc.), the teachings of Lin are quite broad and encompass such possibilities: "The term 'heterologous DNA' refers to DNA which has been transferred from one individual animal, species or breed to a different individual animal, species or breed. The term 'transgenic' refers to cells, tissues, embryos, fetuses or animals which carry one or more transgenes. The term 'chimeric' refers to an embryo, fetus or animal which consists of two or more tissues of different genetic composition." (page 14, parag.0131). Given the breadth of the definitions of Lin, the examiner believes they encompass chimeric avians comprising different species, even though there is no specific embodiment of such an animal in Lin. Rapp et al. also do not specifically teach chimeric avians comprising different species, but do refer to animals made with xenogeneic DNA. The examiner notes that chimeric avians comprising different species have been produced in the art by other means (see Li et al.). Li et al. teach "production of duck-chicken chimeras by transferring blastoderm cells" of ducks into chicken embryos (page 1360). Therefore, the examiner asserts that given the state of the art and the breadth of teachings by Lin and Rapp et al., chimeric avians comprising different species is an obvious variant of the methods of Lin in view of Rapp et al.

Therefore the method as taught by Lin in view of Rapp et al. and further in view of Li et al. would have been *prima facie* obvious over the method of the instant application.

### ***Conclusion***

No claims are allowed.

***Examiner Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**.

The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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*JLE*